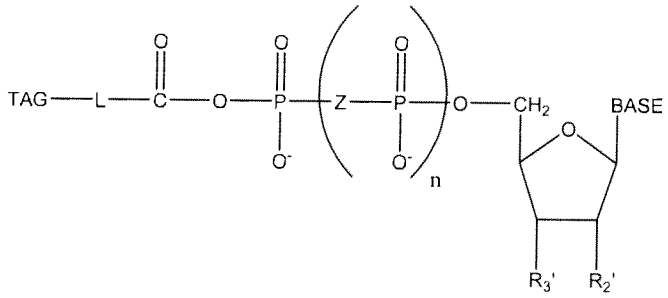
Amendments to the Claims/Listing of Claims

Please amend claims 1, 14 and 20 as follows. In addition, please cancel claim 29 without prejudice. This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (Currently amended) A tagged acyl phosphate or phosphonate probe according to claim 28 wherein X is a nucleotide, such that said probe has the formula:



wherein

BASE is a 5- or 6-membered unsaturated heterocyclic ring comprising from 1 to 3 ring nitrogens, wherein the 5- or 6-membered unsaturated heterocyclic ring is covalently attached through a ring nitrogen to the 1' position of the ribose or deoxy-ribose, wherein the 5- or 6-membered unsaturated heterocyclic ring optionally comprises a 6-membered unsaturated carbocyclic or heterocyclic ring fused thereto, said fused ring comprising from 1 to 2 ring nitrogens, and wherein each carbon position in the BASE may be optionally substituted by a substituent independently selected from the group consisting of -H, -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), =O, acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, or $-(CH_2)_mOH$;

$R_{2'}$ and $R_{3'}$ are independently selected from the group consisting of -H, -OH, -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$, or

$-(CH_2)_m$-phenyl where phenyl is optionally substituted with -F, -Br, -Cl, $-SCH_3$, $-C(O)N(R)(R)$, -CN, $-NO_2$, -N(R)(R), acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$;

n is 0-2;

m is 0 to 6;

TAG is ~~as defined above~~ **a detectable label**;

each Z is independently O, S, NH, or methylene; **[[and]]**

L **is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;** and

each R ~~are as previously defined~~ **is independently H or $-C_{1-6}$ alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure**.

2. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein BASE is a purine.

3. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein BASE is a pyrimidine.

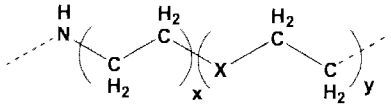
4. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein BASE is selected from the group consisting of adenine, thymine, uracil, guanine, cytosine, inosine, 5-bromouracil, 5-fluorouracil, 2-aminopurine, N^6-cyclohexyl adenine, 8-azaguanine, and 5-fluorocytosine.

5. (Previously presented) A tagged acyl-nucleotide probe according to claim 4, wherein BASE is selected from the group consisting of adenine, thymine, uracil, guanine, and cytosine.

6. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein $R_{2'}$ and $R_{3'}$ are independently H or OH.

7. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein $R_{2'}$ and $R_{3'}$ are each OH.

8. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein L has the structure:

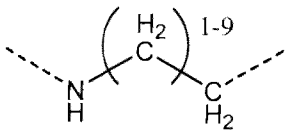


wherein

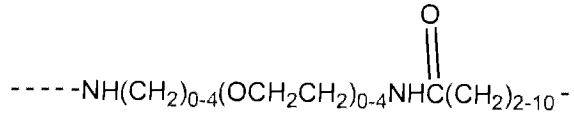
x and y are independently in the range of 0 to 4, and

X is O or CH_2.

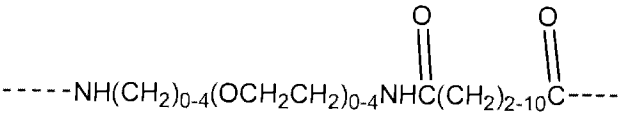
9. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein L has the structure:



;



; or

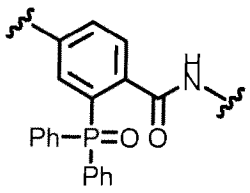


.

10. (Withdrawn) A tagged acyl-nucleotide probe according to claim 8, wherein L has the structure $-NH(CH_2)_2(OCH_2CH_2)_{1-4}-$.

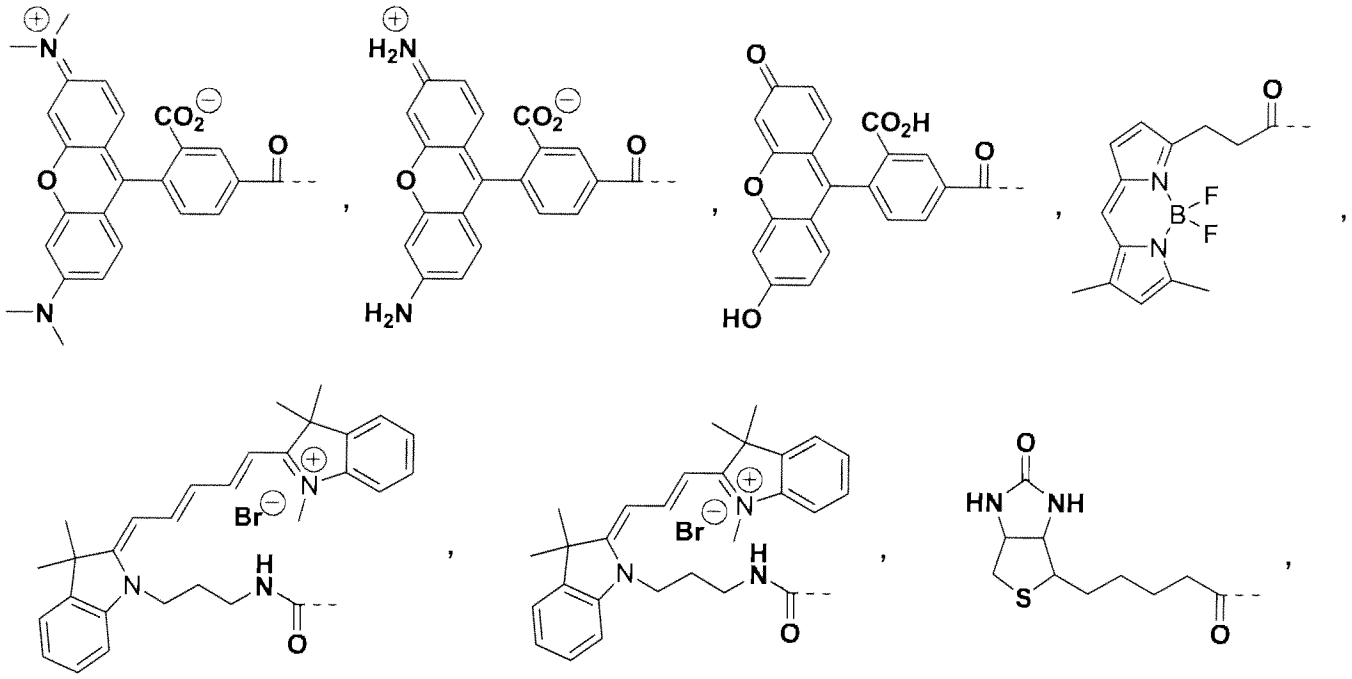
11. (Withdrawn) A tagged acyl-nucleotide probe according to claim 1, wherein L comprises a triazole moiety.

12. (Withdrawn) A tagged acyl nucleotide probe according to claim 1, wherein L comprises the following moiety:



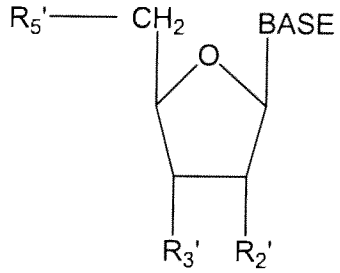
.

13. (Previously presented) A tagged acyl-nucleotide probe according to claim 1, wherein the TAG is selected from the group consisting of:



and dethiobiotin; wherein 5-substituted carboxyrhodamine or 5-substituted carboxyfluorescein may be replaced with 6-carboxyrhodamine or 6-carboxyfluorescein, or with a mixture of 5- and 6- substituted carboxyrhodamine or carboxyfluorescein.

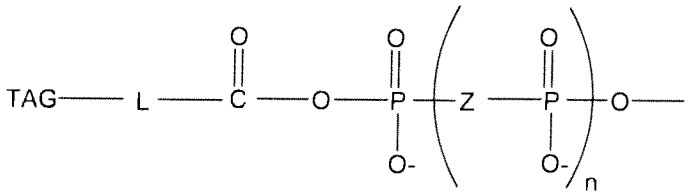
14. (Currently amended) A tagged acyl phosphate or phosphonate probe according to claim 28 wherein X is a nucleotide, such that said probe has the structure:



wherein

BASE is a 5- or 6-membered unsaturated heterocyclic ring comprising from 1 to 3 ring nitrogens, wherein the 5- or 6-membered unsaturated heterocyclic ring is covalently attached through a ring nitrogen to the 1' position of the ribose or deoxy-ribose, wherein the 5- or 6-membered unsaturated heterocyclic ring optionally comprises a 6-membered unsaturated carbocyclic or heterocyclic ring fused thereto, said fused ring comprising from 1 to 2 ring nitrogens, and wherein each carbon position in the BASE may be optionally substituted by a substituent independently selected from the group consisting of -H, -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), =O, acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, or $-(CH_2)_mOH$;

one of $R_{2'}$ and $R_{3'}$ and $R_{5'}$ has the following structure:



and the other two of $R_{2'}$ and $R_{3'}$ and $R_{5'}$ are independently selected from the group consisting of -H, -OH, -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$, or $-(CH_2)_m$-phenyl where phenyl is optionally substituted with -F, -Br, -Cl, $-SCH_3$, -C(O)N(R)(R), -CN, $-NO_2$, -N(R)(R), acetoxy, -C(R)(R)(R), $-OCH_3$, $-OCH_2CH_3$, methylene dioxy, trihalomethyl, trihalomethoxy, $-(CH_2)_mOH$;

n is 0-2;

m is 0 to 6;

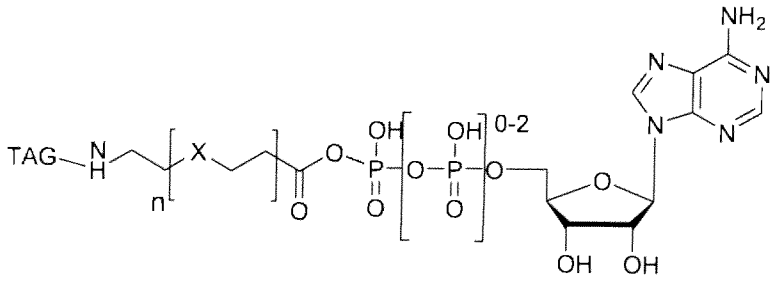
TAG is ~~as defined above~~ **a detectable label**,

each Z is independently O, S, NH, or methylene; **[[and]]**

L **is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;** and

each R ~~are as previously defined~~ **is independently H or $-C_{1-6}$ alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure**.

15. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein

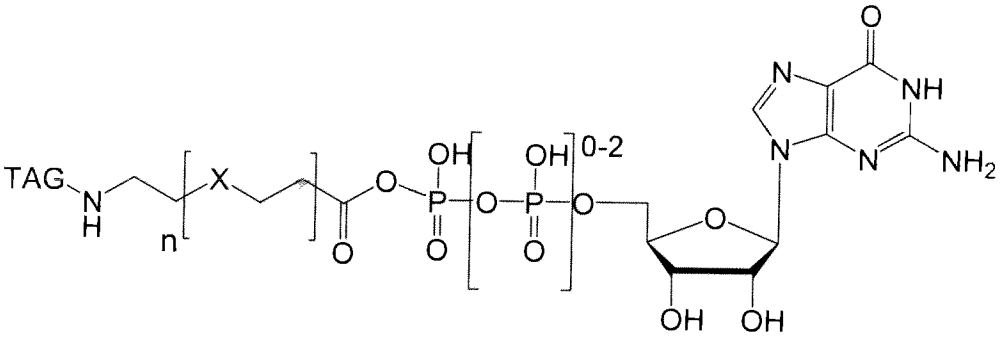
n is 1-4;

X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

16. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein

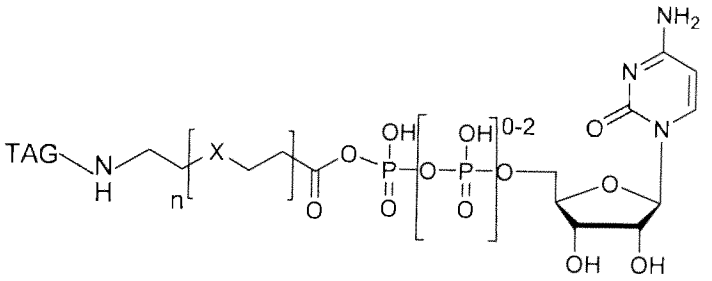
n is 1-4;

X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

17. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein

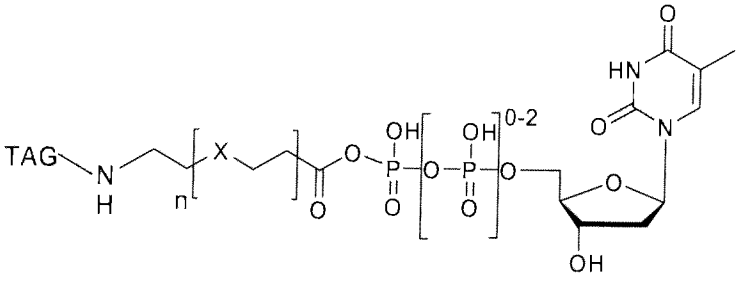
n is 1-4;

X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

18. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein

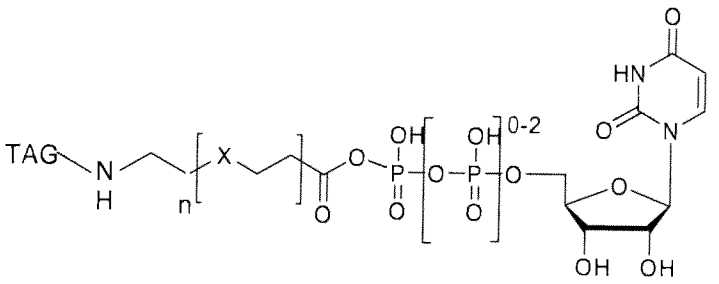
n is 1-4;

X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

19. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein

n is 1-4;

X is O or CH_2; and

TAG is a detectable label;

or a pharmaceutically acceptable salt or complex thereof.

20. (Withdrawn; currently amended) A method for determining the enzyme profile of one or more target proteins in a complex protein mixture, employing one or more probes comprising a nucleotide covalently bound through the terminal phosphate of a 5' mono- di- or tri-phosphate to an acyl group, which is further covalently bound to a TAG via a linker moiety "L", wherein said acyl group forms an adduct with said target protein(s) when said probe is bound to said target protein(s), said method comprising:

combining in a reaction medium said probe(s) and said complex protein mixture under conditions of reaction of said probe(s) with said nucleotide binding protein(s), whereby a conjugate of said probe(s) and said target protein(s) is formed; and

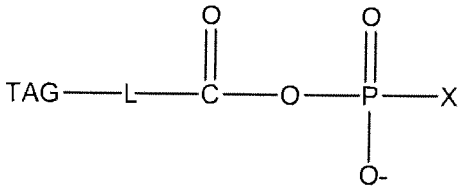
determining said enzyme profile by generating a signal from one or more conjugates formed thereby;

wherein said probe(s) are selected from the nucleotide binding protein-directed probes of one of claims **[[1-18]]** **1-19, 27, 28 or 30-34**.

21. (Withdrawn) A method according to Claim 20, wherein said probe binds to a plurality of target proteins.

22. – 26. (Cancelled)

27. (Previously presented) A tagged acyl phosphate or phosphonate probe having the formula:



wherein

X is an affinity moiety for directing the binding of said TAPP to one or more target proteins linked to the phosphate through an oxygen or carbon;

TAG is a detectable label;

L is an optionally present alkyl or heteroalkyl group of 1-40 backbone atoms selected from the group consisting of -N(R)-, -O-, -S- or -C(R)(R)-, wherein said alkyl or heteroalkyl group optionally includes a carbocyclic or heterocyclic group;

each R is independently H or -C_{1-6} alkyl straight or branched chain, or optionally form an optionally substituted fused carbocyclic or heterocyclic ring structure; and

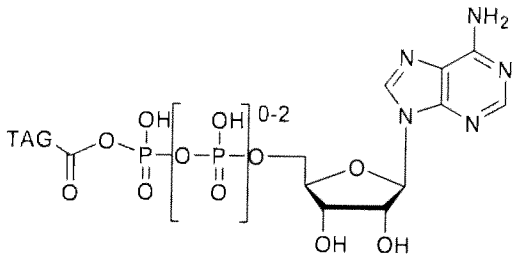
the carbonyl adjacent to L is bound to a carbon to form an acyl group;

or a pharmaceutically acceptable salt or complex thereof.

28. (Original) The tagged acyl phosphate probe of claim 27, wherein X is selected from the group consisting of a nucleotide, nucleotide analogue, optionally substituted naphthyl group, small molecule, steroid, peptide hormone, enzyme cofactor, vitamin, enzyme substrate, lipid, prostaglandin, or receptor ligand.

29. (Cancelled)

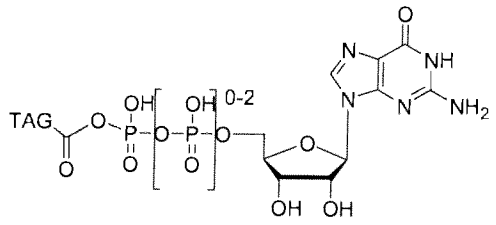
30. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.

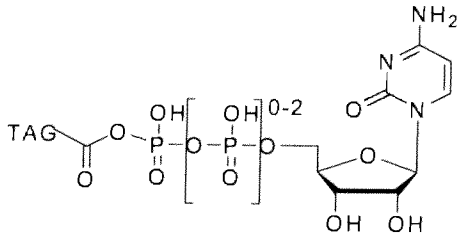
31. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.

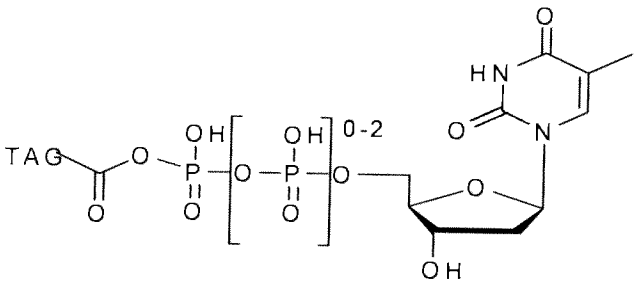
32. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.

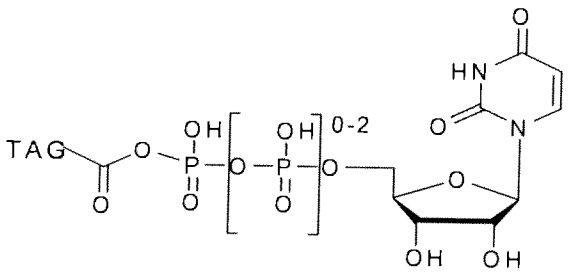
33. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.

34. (Previously presented) A tagged acyl-nucleotide probe having the structure:



wherein TAG is biotin or dethiobiotin;

or a pharmaceutically acceptable salt or complex thereof.